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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,139	12/29/2000	Stephen Quirk	11301-0200 (44039-227522)	1818
7590 08/05/2004			EXAMINER	
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, PA P. O. BOX 2938 MINNEAPOLIS, MN 55402			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 08/05/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/753,139

Applicant(s)

QUIRK ET AL.

Examiner

Malgorzata A. Walicka

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 4,5,8-14,20 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,7,15-19,22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/5/02, 4/30/02 & 6/29/03</u> | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1652

The Response to Restriction Requirement filed July 22, 2004 is acknowledged. Claim 1-23 are pending. Claims 1-3, 7, 15-19 and 22-23 reading on the elected invention and species are the subject of this Office Action.

Detailed Office Action

1. Restriction/election

Applicant's election, with traverse, of Group 1 and species consisting of AFTA linked to SEQ ID NO: 8 in the reply filed on July 22, 2004 is acknowledged. The traversal is on the ground(s) that

"Restriction Requirement is Optional in all cases. M.P.E.P. §803. If the search of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. §803. It is respectfully submitted that the search and examination of the claims can be made without serious burden on the Office" page 1, line 22.

Furthermore, the examiner is reminded,

"M.P.E.P. §803.02 states that 'if the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on merits, even though they are directed to independent and distinct inventions. Accordingly, Applicants respectfully request that the Examiner reconsider whether restriction is proper in this case", page 2, line 5.

Art Unit: 1652

Applicants' arguments have been fully considered but are found not persuasive for the following reasons.

In the Office Action of June 30, 2004 the examiner issued the restriction requirement repeated below.

- I. Claim 1-7, and 15-21 drawn to an MMP regulator comprising a zinc chelator and a TIMP-derived peptide and its composition, classified in class 530, subclass 300.
- II. Claim 8-14, drawn to a method of treating chronic or acute wounds, classified in class 424, subclass 185.1.

In addition, claims 1-23 are generic to a plurality of disclosed patentably distinct species comprising regulators of metalloproteinase consisting of the covalently linked species from group A (zinc chelators) and B (TIMP-derived peptide), wherein each of the groups comprises the following species:

A	B
EDTA	a) 40 sequences described as SEQ ID NO: 1 i.e. Cys Xaa Cys Xaa Pro His Pro
EGTA	b) thousands of seq. described as SEQ ID NO:2, i.e., Xaa Xaa Xaa Xaa XaaThr Xaa Xaa Xaa Xaa Xaa
DTPA	c) thousands of seq. described as SEQ ID NO: 3, i.e., Xaa Xaa Xaa Xaa XaaCys Xaa Xaa Xaa
SDTA	
HEDTA	d) SEQ ID NO: 4
NTA	e) SEQ ID NO: 5

Art Unit: 1652

IDA	f) SEQ ID NO: 6
PSDE	g) SEQ ID NO: 7
AFTA	h) SEQ ID NO: 8
Citric acid	i) SEQ ID NO: 11.
Salicylic acid	
Malic acid	
amino acids	SEQ ID NO: 9
amino acid of	SEQ ID NO: 10

Group I and II are related as product and method of use that can be practiced with another product. Applicants elected Group I directed to product. In the case the product is allowable, pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims directed to the process of using the patentable product, previously withdrawn from consideration as a result of a restriction requirement, are the subject to being rejoined and fully examined for patentability under 37 CFR 1.104.

As to the Markush groups recited by claims 2, 6, 18 and 22 they cover thousands of chemical compounds of different chemical structure, i.e they are not in the proper form. Thus, by no means the members of the Markush group are sufficiently few in number and so closely related that a search and examination of all the claim and species can be made without serious burden. Therefore, restriction as issued in the last Office Action is proper. Claims 1-3, 7, 15-19 and 22-23 drawn to the elected

Art Unit: 1652

invention and species are the subject of examination on merits. Claims 8-14 remain withdrawn from consideration as drawn to the nonelected invention; claims 4-6, 20 and 21 are withdrawn from consideration as directed to nonelected species; see 37 CFR 1.141(b).

2. Objections

2.1. Specification

The specification is objected to for use of the term "chelator". The scope of the invention covers chemical compounds that are not chelators, but nonetheless bind zinc; see page 13, line 3.

Please delete the letter "n" in page 8, line 12.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

2.2. Claims

Please expand all abbreviation recited in the claims for the first time.

Claims are objected to for use of the term "chelator". The scope of the invention covers chemical compounds that are not chelators, but nonetheless bind zinc; for example SEQ ID NOs: 9-10.

Art Unit: 1652

Claims 22, 6, 18 and 22 are objected to because they recite an improper Markush group. Although the recited chemical compounds share the same function of inhibiting metalloproteases, their structure is versatile.

Claim 22 is objected as being dependent on claim 21 that is directed to non-elected species.

Claim 22 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim depends on claim 21 which is directed to a composition of MMP regulator consisting of zinc chelator and TIMP derived peptide comprising SEQ ID NO: 1-3. Claim 22 broadens the scope of claim 21 because it is directed to a MMP regulator comprising SEQ ID NO: 1-8 and 11.

3. Rejections

3.1. 35 USC section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-3, 7 and 15-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants use the term "MMP regulator" which is confusing, because Applicants' invention is directed to MMP inhibitors. For examination purposes it is assumed that the claims are directed to MMP inhibitors.

Claim 22 is confusing as directed to MMP inhibitor that consists of a zinc binding compound and SEQ ID NO: 11. SEQ ID NO: 11 is not disclosed in the application, and thus, it is missing from the sequence listing.

3.2. 35 USC section 112, first paragraph

3.2.1. Lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7 and 15-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to inhibitors of any matrix metalloprotease, wherein the enzyme is from any natural and man-made source. The claims are missing the description of the matrix protease to be inhibited by the claimed inhibitors, because the

Art Unit: 1652

genus of matrix proteases is a large genus and it is unlikely that all matrix metalloprotease share their inhibitors.

Claims 1 and 15 are directed to extremely large genus MMP inhibitors comprising a versatile genus of zinc chelators (zinc binding compounds) and a genus of TIMP-derived peptides. However, the structure of claimed regulators is not sufficiently described in claims and specification.

Providing several members of zinc chelating (or rather zinc binding) compounds as listed above in the first paragraph of this action, does not allow for identifying the whole genus of zinc chelators comprising chemicals of versatile structures. Thus, a zinc-binding compound used for construction of inhibitor should be identified by its structure.

Also the genus of TIMP derived polypeptides is a large a versatile genus for which Applicant have not provided definition. There are several TIMPs in animal bodies (e.g. TIMP-1, - 2, -3) that are about 200 amino acid long. The term polypeptide means in the art a chemical compound consisting of less than 100 amino acid residues. Thus, from each TIMP (natural or man-made) one skilled in the art can select thousands of polypeptides that contain 100 or less amino acid residues. In addition, Applicants do not define what they understand by the term TIMP derived polypeptide. Nowhere in the specification Applicants state which residues of TIMP are considered to form "TIMP derived polypeptide". The elected SEQ ID NO: 8 consists of amino acids 24-28 of human, rabbit, baboon and sheep TIMP-1 and chicken TIMP-3. But this pentapeptide is also a part of fruit fly 95 protein (amino acids 241-245), sea urchin's fibropellin (amino

Art Unit: 1652

acids 542-546) and of macaque's versican (amino acids 742-746), to mention only a few. In addition, Applicants themselves define SEQ ID NO: 1-3, which they use for constructing inhibitors, as definite fragments of MMP not any TIMP (see page 14, line 21 and further, and Table 1). However, they even do not disclose the amino acid sequence of said MMP. Taking into account that there are many matrix metalloproteases, the description "SEQ ID NO:2 spans MMP amino acids 62-73" and similar on page 14 are indefinite.

In summary, the genus of claimed MMP inhibitors comprises thousands of chemical compounds whereas Applicants teach only a few such compounds, i. e., ChePep-1, ChePep-2, ChePep-3, ChePep-4, ChePep-5, ChePep-6 (the elected species) and PSDE covalently linked to SEQ ID NO: 2. Providing one skilled in the art with these representatives of the claimed genus is not sufficient to for identifying structural characteristics of the whole genus.

Claim 2-3, 7, 18-19 and 23 are directed to inhibitors that contain as the zinc chelator AFTA, however, the peptide parts of said inhibitors consist of a genus of thousands of peptides for which the sufficient structural description is lacking in the claims and in the specification.

Claims 16 and 17 are included in this rejection because they are depending on rejected base claim 15 and do not correct its language.

In view of lack of structural description of claimed inhibitors of MMP, or their compositions, Applicants failed to sufficiently describe the claimed invention in such full,

Art Unit: 1652

clear, concise, and exact terms that a skilled artisan would recognize they were in possession of the claimed invention.

3.2.2. *Scope of enablement*

Claims 1- 3, 7 and 15-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ChePep-1 ChePep-2 ChePep-3 ChePep-4 ChePep-5 ChePep-6 (the elected species) and PSDE covalently linked to SEQ ID NO: 2 does not reasonably provide enablement for

- 1) any inhibitor of any MMP that consists of a zinc chelator and a TIMP derived peptide;
- 2) any inhibitor of any MMP that consists of AFTA and a TIMP derived peptide; and
- 3) any inhibitor of any MMP that consists of a zinc chelator and a peptide derived from TIMP that contains at least one cysteine residue.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of inhibitors of MMP covered by subgenera (1) - (3). See also the above rejection for lack of written description.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any inhibitor of any MMP, natural or man-made, wherein said inhibitor consists of:

- 1) any zinc chelator and any TIMP derived peptide;
- 2) AFTA and any TIMP derived peptide; and
- 3) consists of any zinc chelator and any peptide derived from TIMP that contains at least one cysteine residue.

While methods of chemical synthesis and screening for enzyme inhibitors are well known in the relevant art, and skills of the artisans highly developed, preparing inhibitors of any MMP as described under (1)-(3) above is outside the realm of routine experimentation and has a low probability of success. While enablement is not precluded by the necessity for routine manipulation of chemical structure and screening of synthesized chemicals for required function of inhibitors, if a large amount synthesis and screening is required, the specification must provide a reasonable amount of

Art Unit: 1652

guidance with respect to the direction in which the experimentation should proceed so that the claimed species have the functionality of inhibitors of MMP. The provision of several chemical compound called ChePep among them ChePep-6, consisting of AFTA and SEQ ID NO: 8 and being and effecting inhibitor of MMP-9 fails to provide such guidance of inhibitors with major structural variations therefrom which remain encompassed within the scope of the rejected claims.

Without a further guidance on the part of Applicants with regards to the name of MMP to be inhibited and the structure of the claimed inhibitors experimentation left to those in the art is improperly extensive and undue.

4. Conclusion

Claims 1- 3, 7 and 15-23 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (571) 272-0928. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (572) 272-0928. The fax number for this Group is (703) 872-9306.

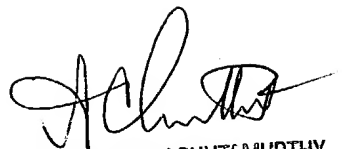
Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Art Unit: 1652

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner



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